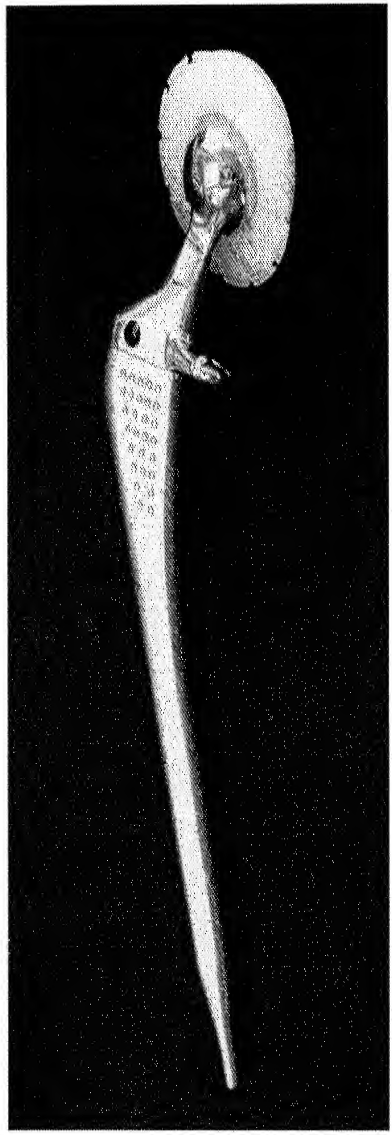
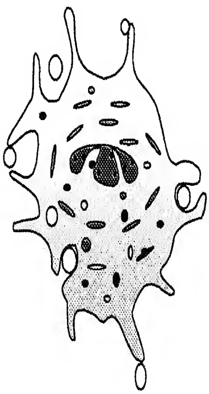

PreOp


PostOp

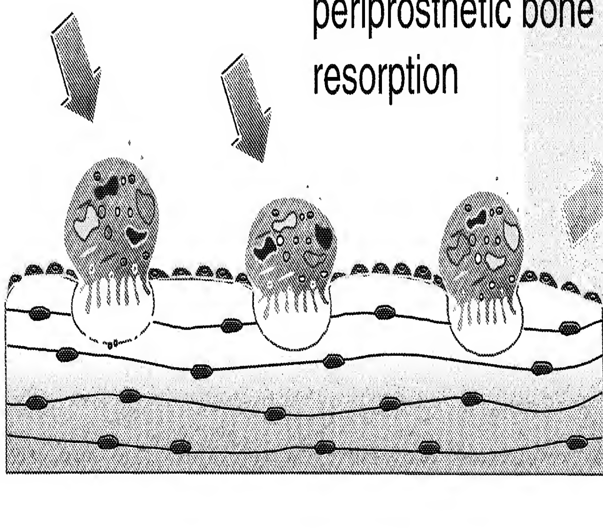


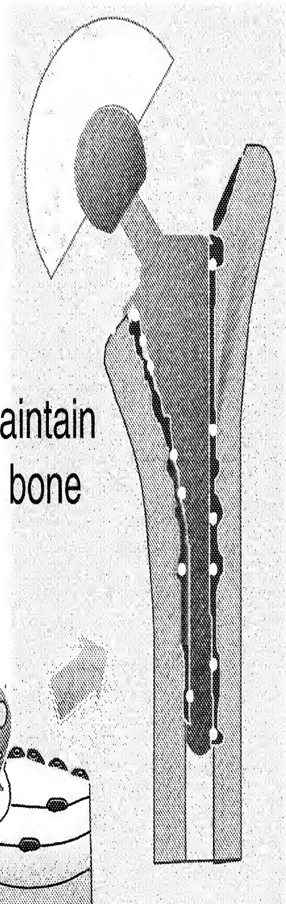
Problem 1: Wear Particle Disease – Osteolysis



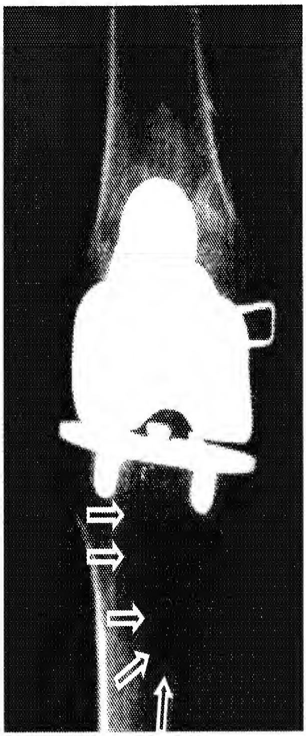
Various cytokines
Collagenase,
Gelatinase

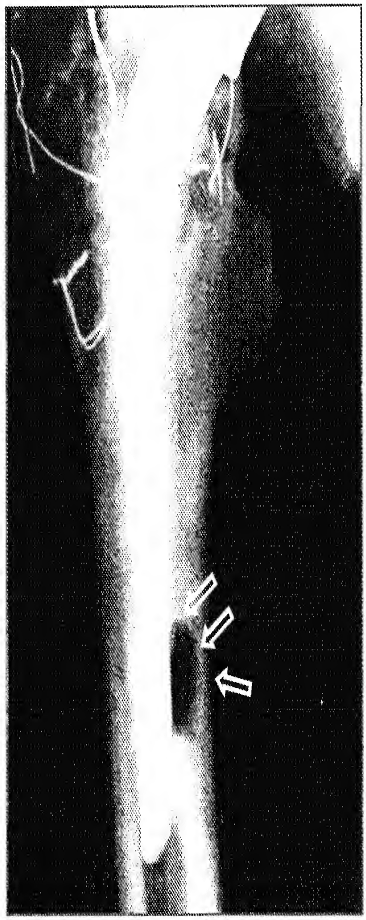
Initiate and maintain
periprosthetic bone
resorption





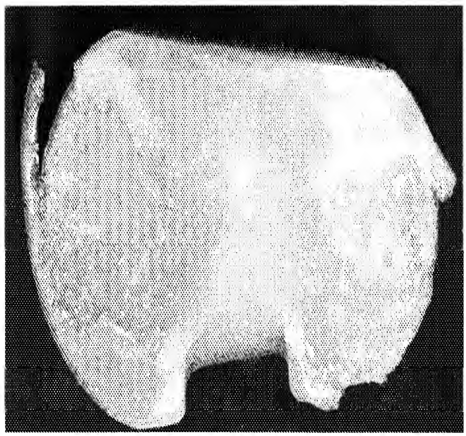
Radiological manifestation of osteolysis



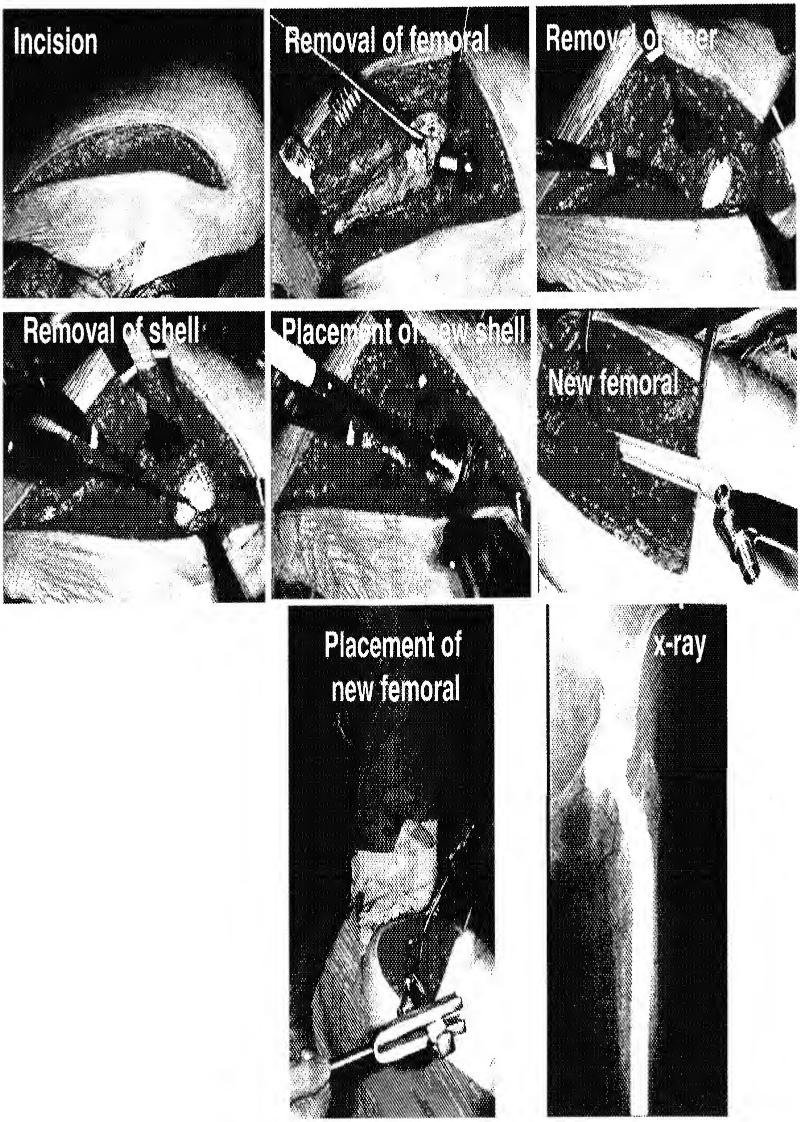


Problem 2: Oxidation Induced Damage

- Terminal gamma sterilization
- Induces residual free radicals
- Which over time causes oxidation of the polymer in vivo



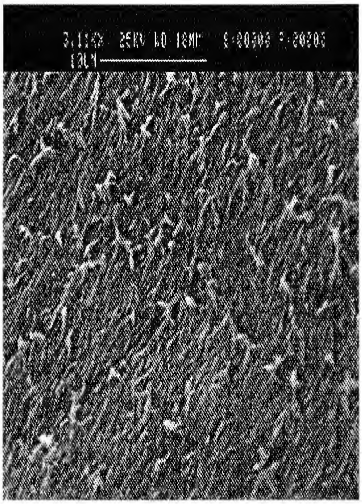
Typical revision hip surgery

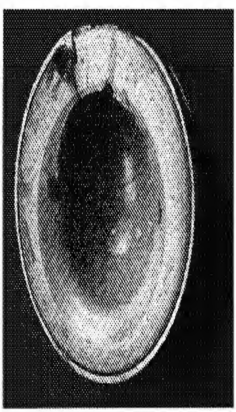


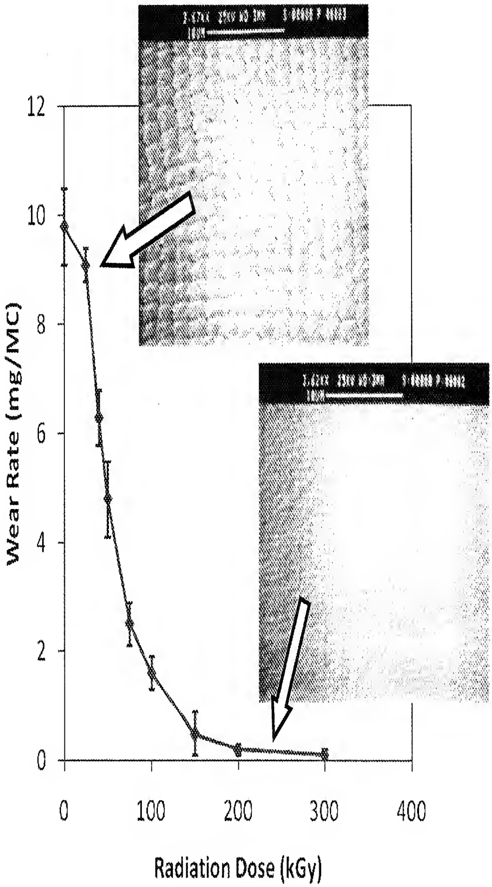
Revision Surgeries are typically caused by WEAR and OXIDATION

AIMS
Improve wear
Improve oxidation

Solution to Wear: Crosslinking

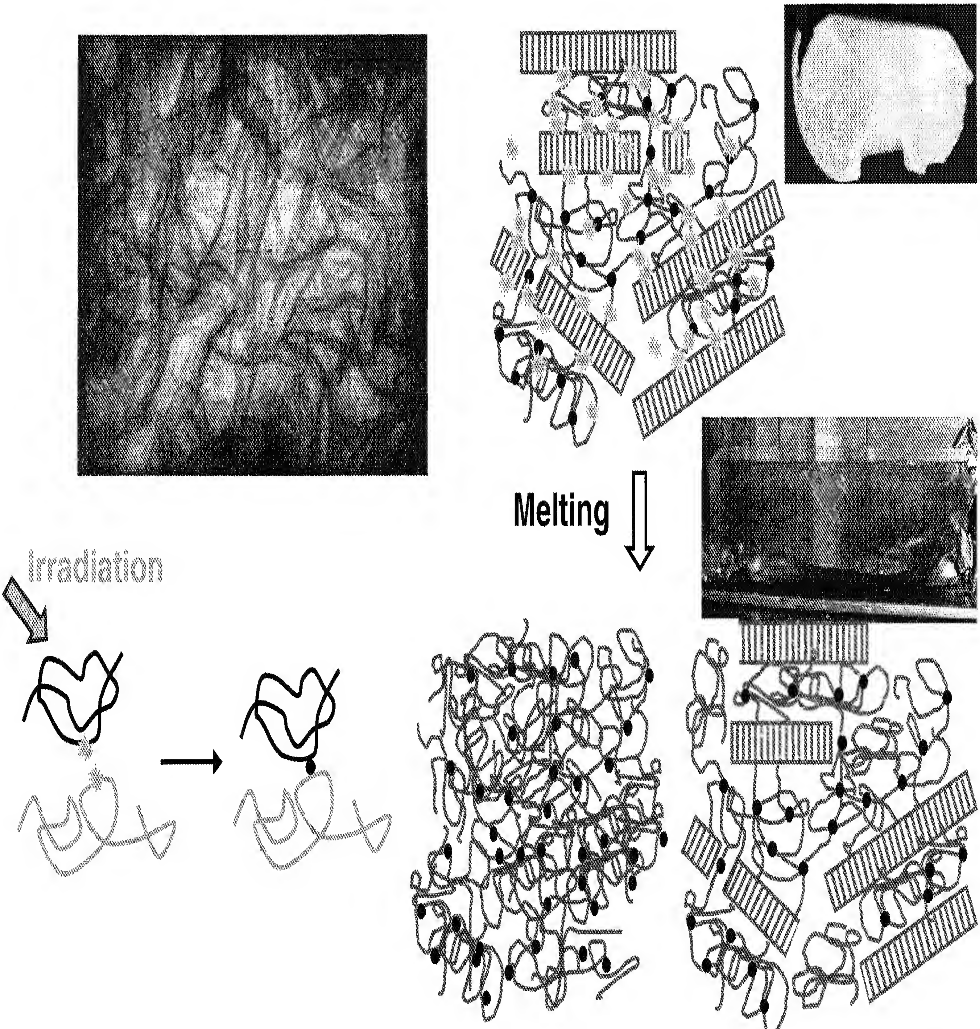






Muratoglu et al., Biomaterials, 20:1463, 1999

Problem: Radiation Induces Oxidation

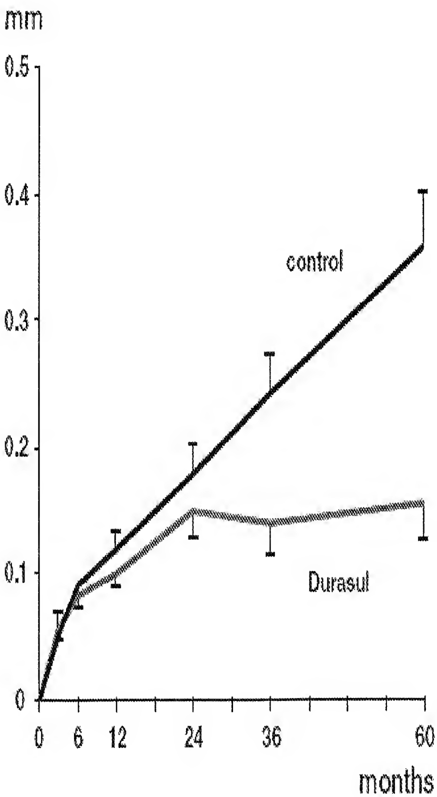


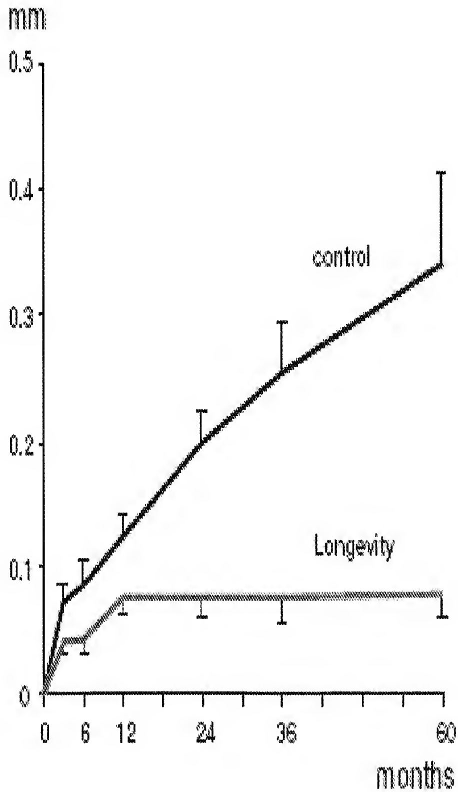
5-year experience of highly cross-linked polyethylene in cemented and uncemented sockets

Two randomized studies using radiostereometric analysis

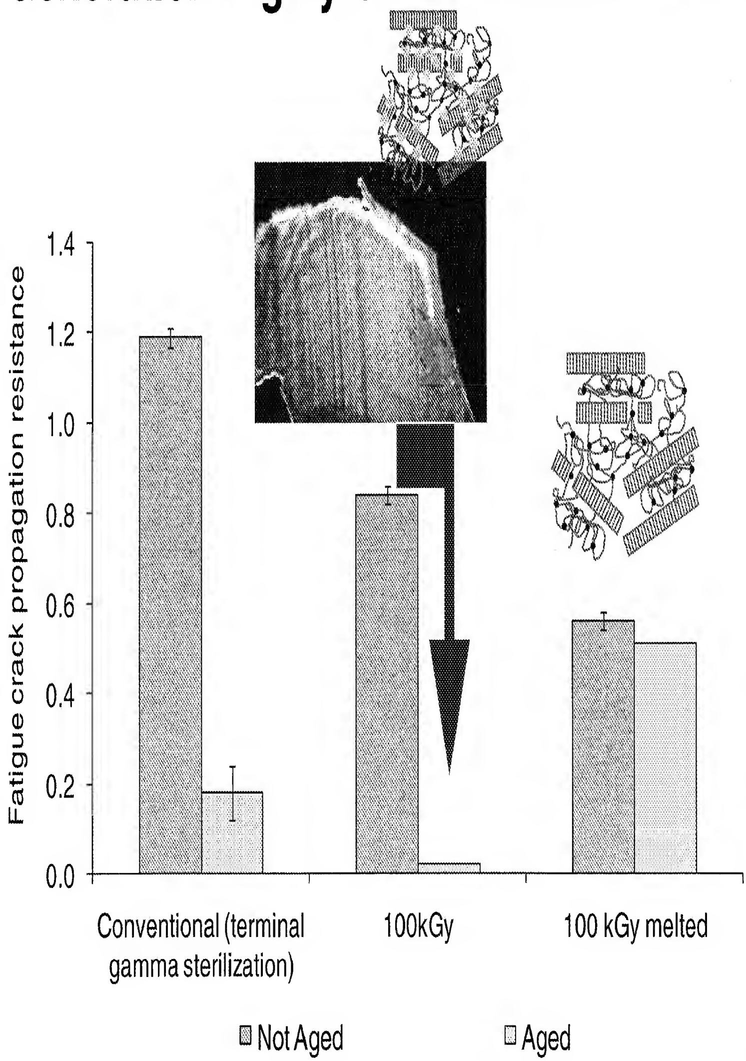
Acta Ortho. (2007)

Georgios Digas, Johan Kärrholm, Jonas Thanner, and Peter Herberts

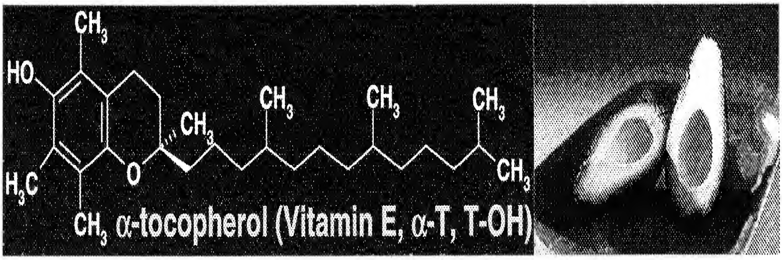




1st Generation Highly Crosslinked UHMWPEs



Use of an antioxidant to stabilize free radicals: Vitamin-E



$R^{\bullet} + O_2 \rightarrow ROO^{\bullet}$

$ROO^{\bullet} + RH \rightarrow ROOH + R^{\bullet}$

Chain reaction cycle leads to oxidation and failure

But with Vitamin-E

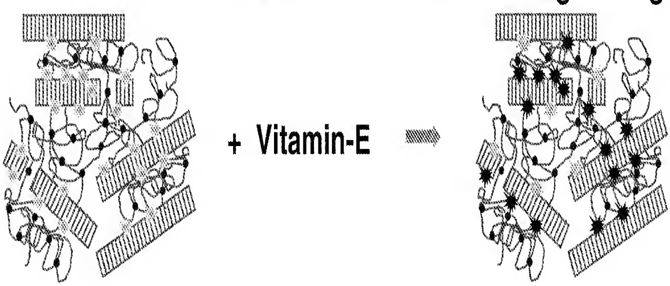
$ROO^{\bullet} + T\text{-}OH \rightarrow ROOH + TO^{\bullet}$ $\cancel{R^{\bullet}}$

Chain reaction cycle is broken by vitamin-E

$T\text{-}O^{\bullet} + TO^{\bullet} \rightarrow TOOT$ dimerization

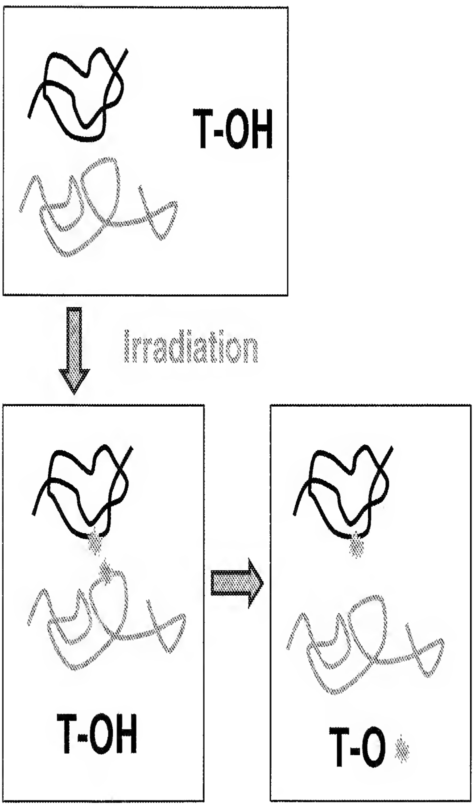
$T\text{-}O^{\bullet} + R^{\bullet} \rightarrow TO\text{-}R$ grafting

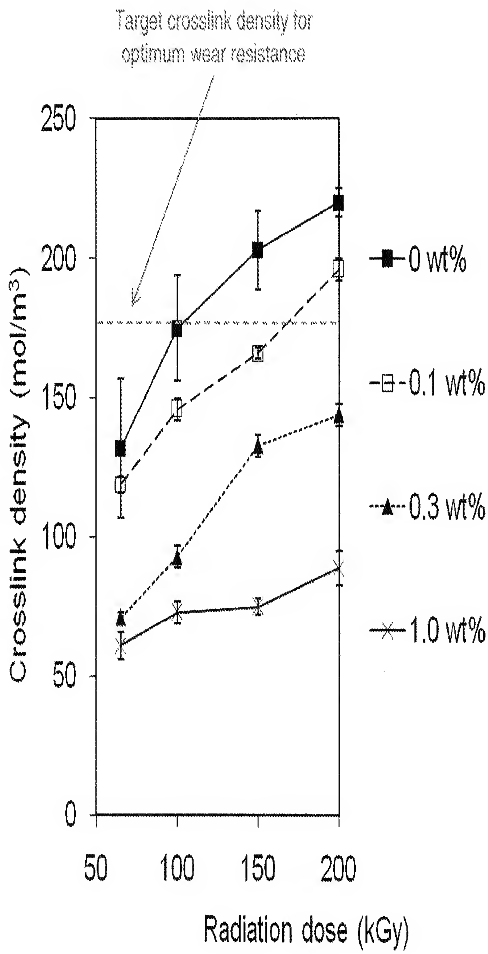
$T\text{-}O^{\bullet} + ROO^{\bullet} \rightarrow TO\text{-}OOR$ grafting



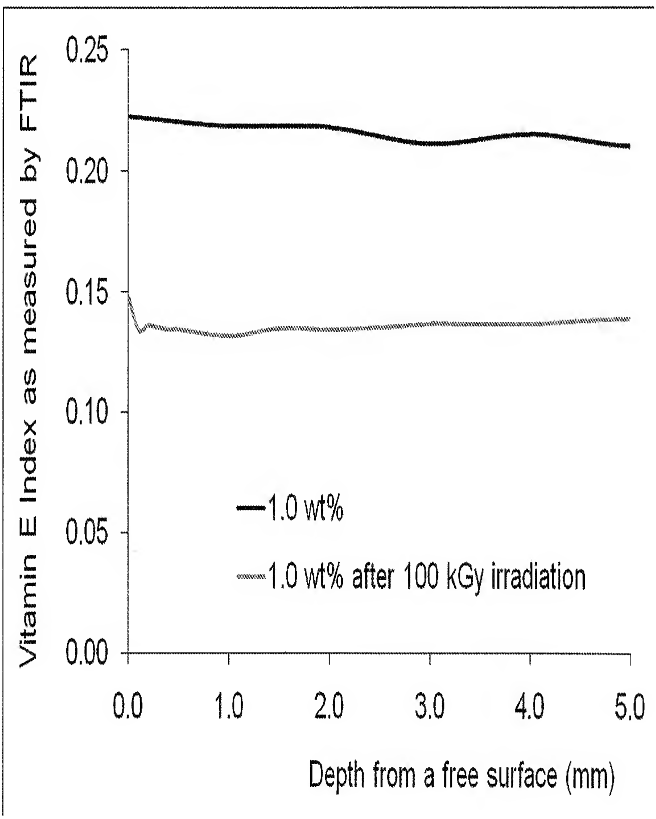
HOWEVER!

- Vitamin-E inhibits crosslinking by radiation

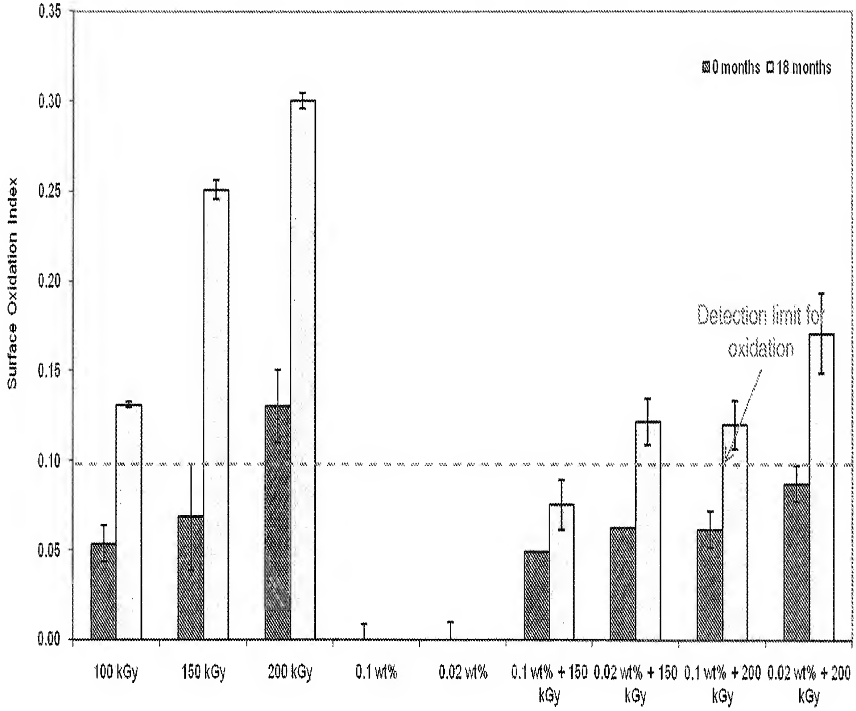




Vitamin E is a free radical scavenger, therefore it reacts with the free radicals on the polyethylene chains in its vicinity. These reactions during radiation deplete some of the vitamin E, which is then not available for preventing polyethylene against oxidation after irradiation.



Oxidation resistance



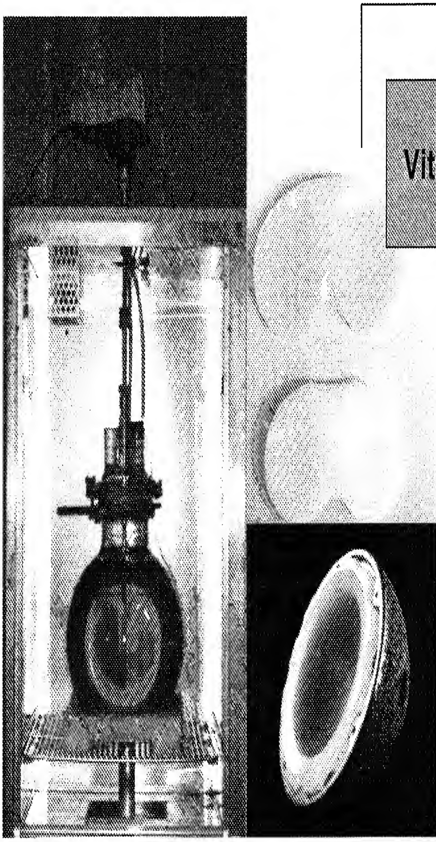
Radiation crosslinked only	Blends with no crosslinking	Room Temperature Radiation Crosslinked Blends

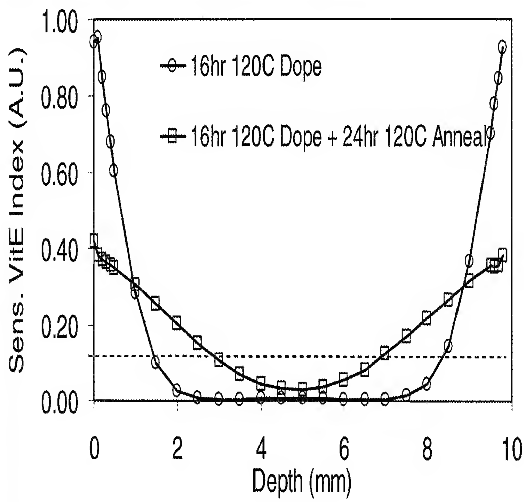
Solution: Antioxidant Doping after Irradiation

UHMWPE stock → Machine → Irradiate

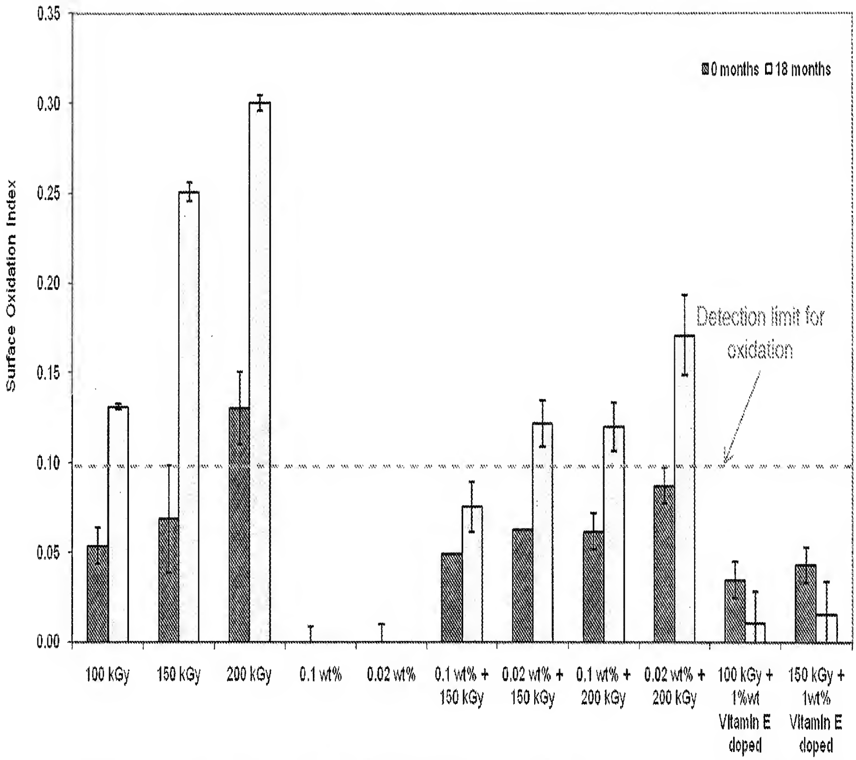
Dope with Vitamin-E

e.g., 120°C Vitamin-E for 16 hours → e.g., Anneal at 120°C in inert for 24 hours → Package and Sterilize



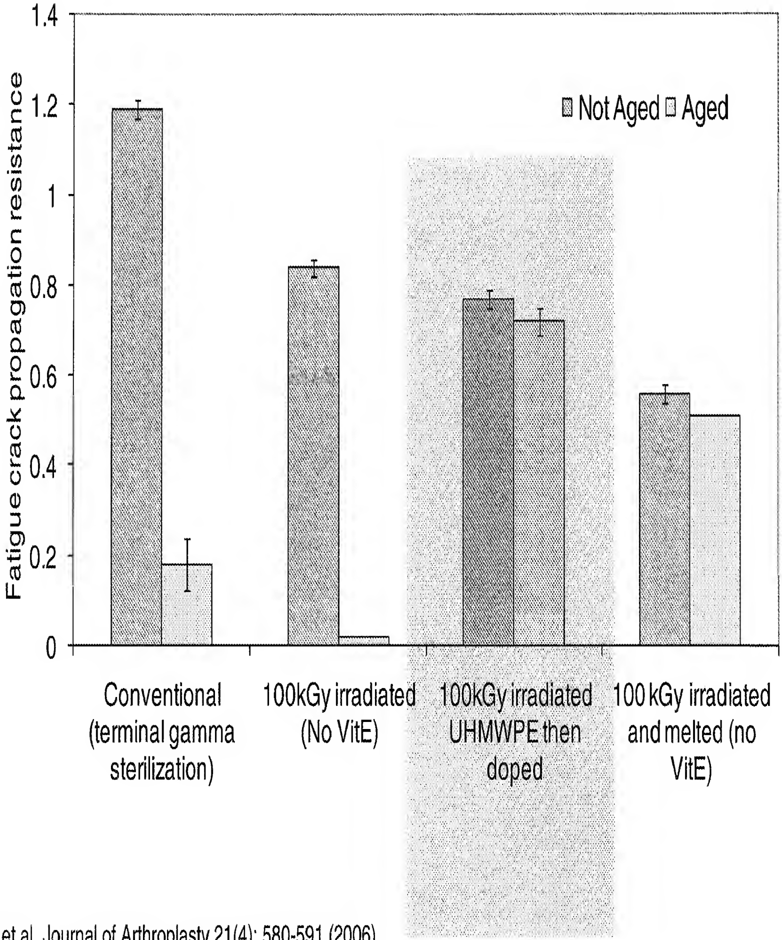


Oxidation resistance: RT Irradiated Blends vs. Irradiated and Doped



Radiation crosslinked only	Blends with no crosslinking	Room Temperature Radiation Crosslinked Blends	Radiation Crosslinked and doped

Fatigue Crack Propagation Resistance



Oral et al. Journal of Arthroplasty 21(4): 580-591 (2006)
Oral et al. Biomaterials 25: 5515-5522 (2004)

Importance of preserving fatigue strength

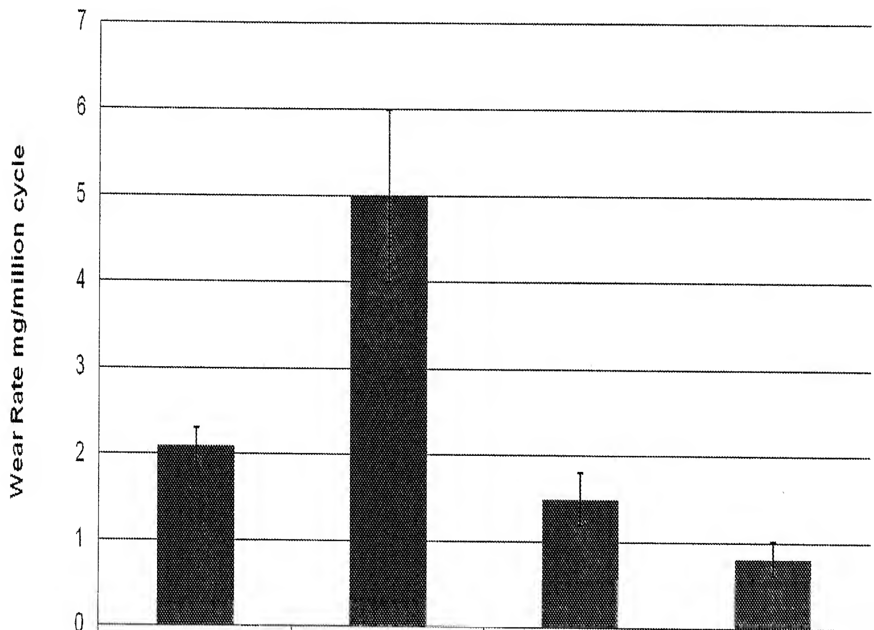
UHMWPE	Unaged fatigue resistance	Aged fatigue resistance	dx (mol/m^3)
Radiation sterilization (25 kGy)	1.20	0.18	60
Radiation (100 kGy)	0.66	NT	175
Radiation (100 kGy) → Melting	0.54	0.51	175
Radiation (100 kGy) → Dope Vit-E (1 wt%)	0.77	0.72	175
1wt% Blend → Radiation (100 kGy)	~1.20	~1.20	73

Post-irradiation melting decreases fatigue strength.

Oxidation drastically reduces fatigue strength.

By using vitamin E doping after irradiation of consolidated UHMWPE, both problems are avoided.

From Examples 4 and 15 in the Specification



0.1wt% Blend 100kGy radiation crosslinked	0.3wt% Blend 100kGy radiation crosslinked	65kGy radiation crosslinked + vitE doped (1wt%) + terminal gamma sterilization	100kGy radiation crosslinked + vitE doped (1wt%) + terminal gamma sterilization
2.1	5	1.5	0.82

All irradiation was at room temperature (RT)

Blends = VitE mixing before consolidation

Prior Art (Lidgren, Parth & Schaffner)

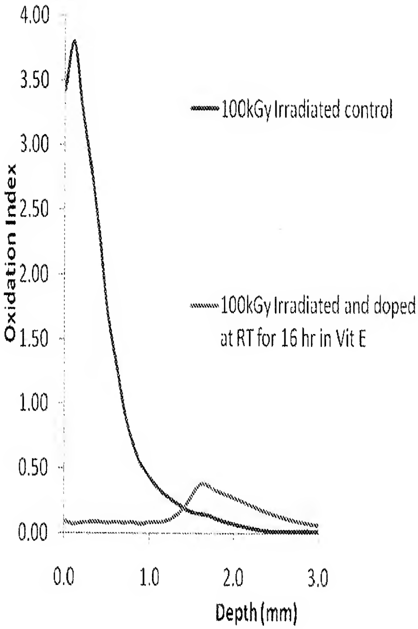
Inhibits crosslinking
Reduces vitE potency

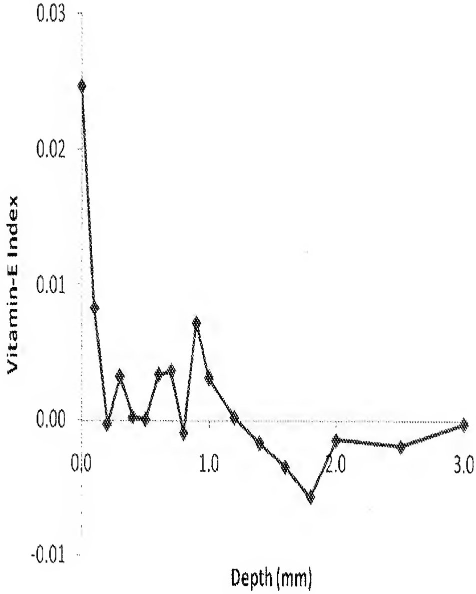
Powder → Blending with VitE → Consolidation → RT Irradiation

Reverse powder treatment

Cannot consolidate
crosslinked powder

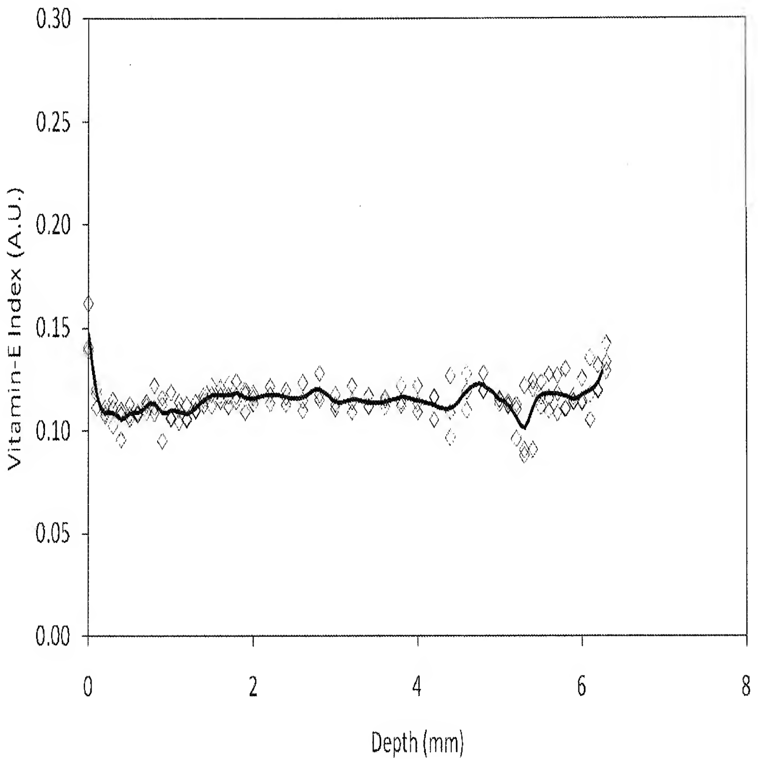
Powder → RT Irradiation → Blending with VitE → Consolidation



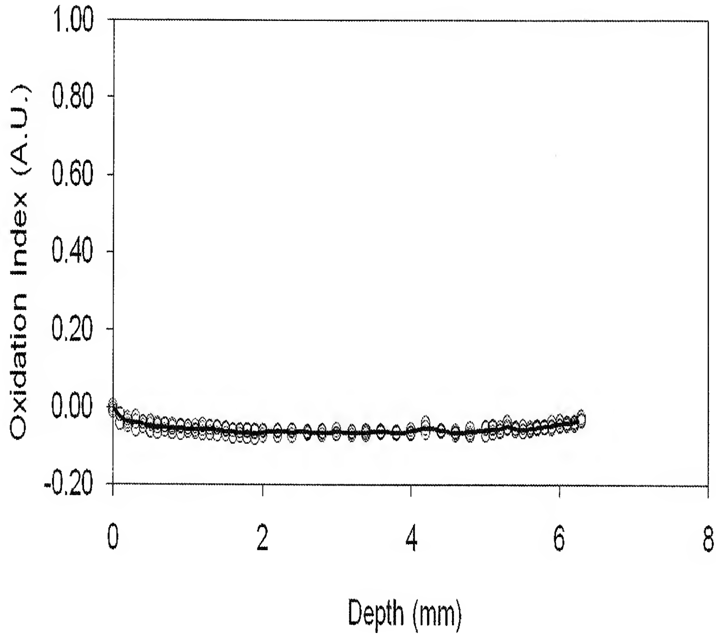


Samples: 100kGy irradiated UHMWPE.

Control (no vitamin E) and doped with vitamin E at room temperature by soaking and then aged in a pressure vessel at 5 atm of O_2 gas at 80° C for 2 weeks. Vitamin E penetration was initially limited (graph on the right) after the doping step, and oxidation was eliminated near the subsurface region where there was vitamin E present, but oxidation started to occur beyond the depth where the vitamin E did not have a detectable presence (graph on left). Annealing to increase the uniformity of vitamin E presence avoids oxidation throughout the sample.



Vitamin E profile of irradiated and then doped and annealed sample (slide 23) that showed no oxidation after oven aging at 80° C. Vitamin E was distributed throughout the sample.



Irradiated and then doped and annealed sample after oven aging at 80° C showed no oxidation because vitamin-E was present throughout the thickness of the sample.